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     (FILE 'HOME' ENTERED AT 12:22:28 ON 03 DEC 2001)

     FILE 'MEDLINE, AGRICOLA, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT
     12:22:38 ON 03 DEC 2001
L1             3 S LYSE AND GLUTAMATE AND COLI
L2          1229 S COLI AND BIOSYNTHESIS AND (GLUTAMATE OR (GLUTAMIC (W) ACID))
L3             2 S L2 AND LYSE
L4           563 S L2 AND (AMINO (W) ACID)
L5           410 DUP REM L4 (153 DUPLICATES REMOVED)
L6           319 S L5 NOT PY>1998
L7           236 S LYSE AND (TRANSMEMBRANE OR EXPORT OR TRANSPORTER)
L8            37 S L7 AND LYSINE
L9            29 DUP REM L8 (8 DUPLICATES REMOVED)
L10            5 S L9 AND (GLUTAMATE OR (GLUTAMIC (W) ACID))
L11           12 S RHT AND (TRANSMEMBRANE OR EXPORT OR TRANSPORTER)
L12            4 DUP REM L11 (8 DUPLICATES REMOVED)
L13          103 S (RHT OR RHT#) AND GLUTAMATE
L14           36 DUP REM L13 (67 DUPLICATES REMOVED)
L15           18 S L14 NOT PY>1999
L16          111 S (RHT OR RHT#) AND (GLUTAMATE OR (GLUTAMIC (W) ACID))
L17           42 DUP REM L16 (69 DUPLICATES REMOVED)
L18           22 S L17 NOT PY>1999

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YOU HAVE REQUESTED DATA FROM 22 ANSWERS - CONTINUE? Y/(N):y

L18 ANSWER 1 OF 22 MEDLINE
ACCESSION NUMBER: 2000027571 MEDLINE
DOCUMENT NUMBER: 20027571 PubMed ID: 10557344
TITLE: Pituitary adenylyl cyclase-activating peptide: a pivotal modulator of glutamatergic regulation of the suprachiasmatic circadian clock.
AUTHOR: Chen D; Buchanan G F; Ding J M; Hannibal J; Gillette M U
CORPORATE SOURCE: Department of Molecular Physiology, University of Illinois at Urbana-Champaign, Urbana, IL 61801, USA.
CONTRACT NUMBER: NS22155 (NINDS)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Nov 9) 96 (23) 13468-73. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991213

AB The circadian clock in the suprachiasmatic nucleus (SCN) of the hypothalamus organizes behavioral rhythms, such as the sleep-wake cycle, on a near 24-h time base and synchronizes them to environmental day and night. Light information is transmitted to the SCN by direct retinal projections via the retinohypothalamic tract (**RHT**). Both **glutamate** (Glu) and pituitary adenylyl cyclase-activating peptide (PACAP) are localized within the **RHT**. Whereas Glu is an established mediator of light entrainment, the role of PACAP is unknown. To understand the functional significance of this colocalization, we assessed the effects of nocturnal Glu and PACAP on phasing of the circadian rhythm of neuronal firing in slices of rat SCN. When coadministered, PACAP blocked the phase advance normally induced by Glu during late night. Surprisingly, blocking PACAP neurotransmission, with either PACAP6-38, a specific PACAP receptor antagonist, or anti-PACAP antibodies, augmented the Glu-induced phase advance. Blocking PACAP in vivo also potentiated the light-induced phase advance of the rhythm of hamster wheel-running activity. Conversely, PACAP enhanced the Glu-induced delay in the early night, whereas PACAP6-38 inhibited it. These results reveal that PACAP is a significant component of the Glu-mediated light-entrainment pathway. When Glu activates the system, PACAP receptor-mediated processes can provide gain control that generates graded phase shifts. The relative strengths of the Glu and PACAP signals together may encode the amplitude of adaptive circadian behavioral responses to the natural range of intensities of nocturnal light.

L18 ANSWER 2 OF 22 MEDLINE
ACCESSION NUMBER: 2000019375 MEDLINE
DOCUMENT NUMBER: 20019375 PubMed ID: 10553947
TITLE: Electrophysiological evidence for the role of substance P in retinohypothalamic transmission in the rat.
AUTHOR: Kim Y I; Kim S H; Kim D Y; Lee H W; Shin H C; Chung J M; Han H C; Na H S; Hong S K
CORPORATE SOURCE: Department of Physiology and Neuroscience Research Institute, Korea University College of Medicine, Seoul, South Korea.. yikim@kuccnx.korea.ac.kr
SOURCE: NEUROSCIENCE LETTERS, (1999 Oct 22) 274 (2) 99-102. Journal code: N7N; 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991206

AB The retinohypothalamic tract (**RHT**) is a neural pathway through which photic time cues are delivered directly to the mammalian circadian pacemaker in the suprachiasmatic nucleus (SCN). Although the excitatory amino acid **glutamate** is the primary neurotransmitter in the **RHT**, other substances such as substance P (SPq also have been suggested to play a role. The present study tested the hypothesis that SP participates in retinohypothalamic transmission and selectively modulates either N-methyl-D-aspartate (NMDA) or non-NMDA receptor-mediated neurotransmission. The SP antagonist L-703,606 depressed the excitatory postsynaptic current (EPSC) evoked by optic nerve stimulation in SCN neurons in rat hypothalamic slices. The SP antagonist also had a similar depressive effect on the NMDA and non-NMDA receptor-mediated components of the EPSC. These results suggest that SP is an excitatory neuromodulator

contributing to the expression of both the NMDA and non-NMDA receptor-mediated components of retinohypothalamic transmission.

L18 ANSWER 3 OF 22 MEDLINE
ACCESSION NUMBER: 1999439021 MEDLINE
DOCUMENT NUMBER: 99439021 PubMed ID: 10511003
TITLE: Serotonin modulation of calcium transients in cells in the suprachiasmatic nucleus.
AUTHOR: Flett J; Colwell C S
CORPORATE SOURCE: Mental Retardation Research Center, Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles 90024-1759, USA.
SOURCE: JOURNAL OF BIOLOGICAL RHYTHMS, (1999 Oct) 14 (5) 354-63. Journal code: A9L; 8700115. ISSN: 0748-7304.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991102

AB Information about environmental lighting conditions is conveyed to the suprachiasmatic nucleus (SCN), at least in part, via a glutamatergic fiber pathway originating in the retina, known as the retinohypothalamic tract (**RHT**). Previous work indicates that serotonin (5HT) can inhibit this pathway, although the underlying mechanisms are unknown. The authors became interested in the possibility that 5HT can inhibit the glutamatergic regulation of Ca2+ in SCN neurons and, by this mechanism, modulate light-induced phase shifts of the circadian system. To start to examine this hypothesis, optical techniques were used to measure Ca2+ levels in SCN cells in a brain slice preparation. First, it was found that 5HT produced a reversible and significant inhibition of Ca2+ transients evoked by synaptic stimulation. Next, it was found that 5HT did not alter the magnitude or duration of Ca2+ transients evoked by the bath application of **glutamate** or N-methyl-D-aspartate acid (NMDA) in the presence of tetrodotoxin (TTX). The authors feel that the simplest explanation for these results is that 5HT can act presynaptically at the **RHT**/SCN synaptic connection to inhibit the release of **glutamate**. The demonstration that 5HT can have a dramatic modulatory action on synaptic-evoked Ca2+ transients measured in SCN neurons adds support to the notion that the serotonergic innervation of the SCN may function to regulate environmental input to the circadian system. In addition, it was found that the administration of higher concentrations of 5HT can increase Ca2+ in at least a subpopulation of SCN neurons. This effect of 5HT was concentration dependent and blocked by a broad-spectrum 5HT antagonist (metergoline). In addition, both TTX and the gamma-amino-N-butyric acid (GABA) receptor blocker bicuculline inhibited the 5HT-induced Ca2+ transients. Therefore, the interpretation of this data is that 5HT can act within the SCN to alter GABAergic activity and, by this mechanism, cause changes in intracellular Ca2+. It is also suggested that this 5HT-induced Ca2+ increase might play a role in 5HT-induced phase shifts of the SCN circadian oscillator.

L18 ANSWER 4 OF 22 MEDLINE
ACCESSION NUMBER: 1999088091 MEDLINE
DOCUMENT NUMBER: 99088091 PubMed ID: 9870951
TITLE: Pituitary adenylate cyclase-activating polypeptide and melatonin in the suprachiasmatic nucleus: effects on the calcium signal transduction cascade.
AUTHOR: Kopp M D; Schomerus C; Dehghani F; Korf H W; Meissl H
CORPORATE SOURCE: Dr. Senckenbergische Anatomie, Anatomisches Institut II, Johann Wolfgang Goethe-Universitat, D-60590 Frankfurt, Germany.
SOURCE: JOURNAL OF NEUROSCIENCE, (1999 Jan 1) 19 (1) 206-19. Journal code: JDF; 8102140. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 20000303
Entered Medline: 19990205

AB The suprachiasmatic nucleus (SCN) harbors an endogenous oscillator generating circadian rhythms that are synchronized to the external light/dark cycle by photic information transmitted via the retinohypothalamic tract (**RHT**). The **RHT** has recently been shown to contain pituitary adenylate cyclase-activating polypeptide (PACAP) as neurotransmitter/neuromodulator. PACAPergic effects on cAMP-mediated signaling events in the SCN are restricted to distinct time windows and sensitive to melatonin. In neurons isolated from the SCN of

neonatal rats we investigated by means of the fura-2 technique whether PACAP and melatonin also influence the intracellular calcium concentration ([Ca2+]i). PACAP elicited increases of [Ca2+]i in 27% of the analyzed neurons, many of which were also responsive to the **RHT** neurotransmitters **glutamate** and/or substance P. PACAP-induced changes of [Ca2+]i were independent of cAMP, because they were not mimicked by forskolin or 8-bromo-cAMP. PACAP caused G-protein- and phospholipase C-mediated calcium release from inositol-trisphosphate-sensitive stores and subsequent protein kinase C-mediated calcium influx, demonstrated by treatment with GDP-beta-S, neomycin, U-73122, calcium-free saline, thapsigargin, bisindolylmaleimide, and chelerythrine. The calcium influx was insensitive to antagonists of voltage-gated calcium channels of the L-, N-, P-, Q- and T-type (diltiazem, nifedipine, verapamil, omega-conotoxin, omega-agatoxin, amiloride). Immunocytochemical characterization of the analyzed cells revealed that >50% of the PACAP-sensitive neurons were GABA-immunopositive. Our data demonstrate that in the SCN PACAP affects the [Ca2+]i, suggesting that different signaling pathways (calcium as well as cAMP) are involved in PACAPergic neurotransmission or neuromodulation. Melatonin did not interfere with calcium signaling, indicating that in SCN neurons the hormone primarily affects the cAMP signaling pathway.

L18 ANSWER 5 OF 22 MEDLINE
ACCESSION NUMBER: 1999084073 MEDLINE
DOCUMENT NUMBER: 99084073 PubMed ID: 9866841
TITLE: Physiological, pharmacological and molecular aspects of mammalian biological clocks.
AUTHOR: Akiyama M; Moriya T; Shibata S
CORPORATE SOURCE: Department of Pharmacology, School of Human Sciences, Waseda University, Saitama, Japan.
SOURCE: NIPPON YAKURIGAKU ZASSHI. FOLIA PHARMACOLOGICA JAPONICA, (1998 Oct) 112 (4) 243-50. Ref: 31
Journal code: F2X; 0420550. ISSN: 0015-5691.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 19990223
Entered Medline: 19990210

AB Circadian rhythm is an endogenous rhythm that persists in constant conditions with a period of nearly but not identical to 24 hr. Under natural conditions, the circadian clock is precisely entrained to the daily (24 hr) cycle, because environmental stimulus (especially light) induces a phase shift of the clock. In mammals, the suprachiasmatic nucleus (SCN) of the hypothalamus has been shown to be the primary pacemaker that drives daily rhythms of behavioral and physiological activity. Photic information is conveyed from the retina to the SCN directly by the retinohypothalamic tract (**RHT**) and indirectly by the geniculo-hypothalamic tract (GHT). The transmitter of the **RHT** is **glutamate**, while the GHT is GABA and neuropeptide Y. Serotonergic innervation from the median raphe and melatonin from the pineal body are likely to provide non-photic information to the SCN. Single gene mutations that dramatically alter circadian phenotype were found in the hamster (tau) and mouse (clock). Moreover, the homologous genes of the Drosophila clock gene, per, were found in mammals and the homologue of the mammalian clock was found in Drosophila. These data suggest that the some constitutes of the biological clock may be conserved between Drosophila and mammals, and a transcription-translation feedback loop involving some clock gene products may be a oscillator itself.

L18 ANSWER 6 OF 22 MEDLINE
ACCESSION NUMBER: 1999071308 MEDLINE
DOCUMENT NUMBER: 99071308 PubMed ID: 9852576
TITLE: CREB in the mouse SCN: a molecular interface coding the phase-adjusting stimuli light, **glutamate**, PACAP, and melatonin for clockwork access.
AUTHOR: von Gall C; Duffield G E; Hastings M H; Kopp M D; Dehghani F; Korf H W; Stehle J H
CORPORATE SOURCE: Dr. Senckenbergische Anatomie, Anatomisches Institut II, Johann Wolfgang Goethe-Universitat, D-60590 Frankfurt, Germany.
SOURCE: JOURNAL OF NEUROSCIENCE, (1998 Dec 15) 18 (24) 10389-97.
Journal code: JDF; 8102140. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902

ENTRY DATE: Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990225

AB The suprachiasmatic nucleus (SCN) is a central pacemaker in mammals, driving many endogenous circadian rhythms. An important pacemaker target is the regulation of a hormonal message for darkness, the circadian rhythm in melatonin synthesis. The endogenous clock within the SCN is synchronized to environmental light/dark cycles by photic information conveyed via the retinohypothalamic tract (**RHT**) and by the nocturnal melatonin signal that acts within a feedback loop. We investigated how melatonin intersects with the temporally gated resetting actions of two **RHT** transmitters, pituitary adenylate cyclase-activating polypeptide (PACAP) and **glutamate**. We analyzed immunocytochemically the inducible phosphorylation of the transcription factor Ca2+/cAMP response element-binding protein (CREB) in the SCN of a melatonin-proficient (C3H) and a melatonin-deficient (C57BL) mouse strain. In vivo, light-induced phase shifts in locomotor activity were consistently accompanied by CREB phosphorylation in the SCN of both strains. However, in the middle of subjective nighttime, light induced larger phase delays in C57BL than in C3H mice. In vitro, PACAP and **glutamate** induced CREB phosphorylation in the SCN of both mouse strains, with PACAP being more effective during late subjective daytime and **glutamate** being more effective during subjective nighttime. Melatonin suppressed PACAP- but not **glutamate**-induced phosphorylation of CREB. The distinct temporal domains during which **glutamate** and PACAP induce CREB phosphorylation imply that during the light/dark transition the SCN switches sensitivity between these two **RHT** transmitters. Because these temporal domains are not different between C3H and C57BL mice, the sensitivity windows are set independently of the rhythmic melatonin signal.

L18 ANSWER 7 OF 22 MEDLINE
ACCESSION NUMBER: 1999004201 MEDLINE
DOCUMENT NUMBER: 99004201 PubMed ID: 9787933
TITLE: Photic entrainment of circadian rhythms in rodents.
AUTHOR: Rea M A
CORPORATE SOURCE: Biological Rhythms and Integrative Neuroscience Institute, Air Force Research Laboratory, Brooks AFB, Texas, USA.. rmea@alcft.brooks.af.mil
SOURCE: CHRONOBIOLOGY INTERNATIONAL, (1998 Sep) 15 (5) 395-423. Ref: 227
Journal code: CYT; 8501362. ISSN: 0742-0528.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19990107

AB Photic entrainment of circadian rhythms occurs as a consequence of daily, light-induced adjustments in the phase and period of the suprachiasmatic nuclei (SCN) circadian clock. Photic information is acquired by a unique population of retinal photoreceptors, processed by a distinct subset of retinal ganglion cells, and conveyed to the SCN through the retinohypothalamic tract (**RHT**). **RHT** neurotransmission is mediated by the release of the excitatory amino acid **glutamate** and appears to require the activation of both NMDA- and non-NMDA-type **glutamate** receptors, the expression of immediate early genes (IEGs), and the synthesis and release of nitric oxide. In addition, serotonin appears to regulate the response of the SCN circadian clock to light through postsynaptic 5-HT1A or 5-ht7 receptors, as well as presynaptic 5-HT1B heteroreceptors on **RHT** terminals.

L18 ANSWER 8 OF 22 MEDLINE
ACCESSION NUMBER: 97215281 MEDLINE
DOCUMENT NUMBER: 97215281 PubMed ID: 9061646
TITLE: Membrane properties and synaptic inputs of suprachiasmatic nucleus neurons in rat brain slices.
AUTHOR: Jiang Z G; Yang Y; Liu Z P; Allen C N
CORPORATE SOURCE: Centre for Research on Occupational and Environmental Toxicology, Oregon Health Sciences University, Portland 97201-3098, USA.. Jiang:jiangz@ohsu.edu
CONTRACT NUMBER: 1PO1AG10794 (NIA)
SOURCE: JOURNAL OF PHYSIOLOGY, (1997 Feb 15) 499 (Pt 1) 141-59.
Journal code: JQV; 0266262. ISSN: 0022-3751.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970605

AB 1. Whole-cell recordings were made from 390 neurons of the suprachiasmatic nucleus (SCN) in horizontal brain slices during different portions of the circadian day. The locomotor activity of the rats was measured prior to the preparation of brain slices to insure that each rat was entrained to a 12 h-12 h light-dark cycle. 2. The mean input conductance was 42% higher (1.58 nS) in neurons recorded near the subjective dawn than those (1.11 nS) recorded near the subjective dusk. The current required to hold the neurons at -60 mV also showed a circadian variation with a peak in the middle of the subjective day and a nadir in the middle of the subjective night. Analysis of the variations in the input conductance and the holding current at -60 mV suggested that at least two ion conductances are involved in the pacemaking of the circadian rhythms. 3. Voltage-clamped SCN neurons often had both outward and inward spontaneous postsynaptic currents. The outward currents were blocked by bicuculline but not by strychnine, and were identified as IPSCs mediated by GABAA receptors. The inward currents were blocked by 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX) and were identified as EPSCs mediated by **glutamate**. Most spontaneous synaptic currents were miniature currents but action potential-dependent large events were seen more often in IPSCs than in EPSCs. 4. Stimulation of the optic nerve or chiasm usually evoked a monosynaptic EPSC which was mediated by both NMDA and non-NMDA receptors. In 13% of cells, optic nerve stimulation evoked an outward current or an inward current followed by an outward current; all the evoked currents were blocked by 4-aminophosphonovaleric acid (APV) and CNQX whereas the outward current only was blocked by bicuculline, suggesting involvement of an inhibitory interneuron. 5. SCN neurons sum the excitatory inputs from both optic nerves; on average each SCN cell receives innervation from at least 4.8 retinohypothalamic tract (**RHT**) axons. 6. Focal stimulation in the vicinity of the recorded neuron revealed that nearly all SCN neurons receive local or extranuclear GABAergic inputs operating via GABAA receptors. The EPSCs activated by such stimulation were not significantly different in amplitude and pharmacological properties from those induced by **RHT** stimulation. 7. One hundred and one neurons were labelled with neurobiotin during whole-cell recording. Based on the dendritic structures, four types of SCN neurons (monopolar, radial, simple bipolar and curly bipolar) were identified. The curly bipolar cells had a higher membrane conductance, holding current and hyperpolarization-activated current (Ih) amplitude than the other neuronal types. Radial neurons did not respond to optic nerve stimulation, which activated EPSCs in the other cell types.

L18 ANSWER 9 OF 22 MEDLINE
ACCESSION NUMBER: 97127112 MEDLINE
DOCUMENT NUMBER: 97127112 PubMed ID: 8971980
TITLE: The role of **glutamate** in the photic regulation of the suprachiasmatic nucleus.
AUTHOR: Ebling F J
CORPORATE SOURCE: Department of Anatomy, University of Cambridge, U.K.
SOURCE: PROGRESS IN NEUROBIOLOGY, (1996 Oct) 50 (2-3) 109-32. Ref: 209
Journal code: Q3R; 0370121. ISSN: 0301-0082.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970314

AB Endogenous circadian rhythms govern most aspects of physiology and behaviour in mammals, including body temperature, autonomic and endocrine function, and sleep-wake cycles. Such rhythms are generated by the suprachiasmatic nucleus of the hypothalamus (SCN), but are synchronised to the environmental light-dark cycle by photic cues perceived by the retina and conveyed to the SCN via the retinohypothalamic tract (**RHT**). This review considers many lines of evidence from diverse experimental approaches indicating that the **RHT** employs **glutamate** (or a related excitatory amino acid) as a neurotransmitter. Ultrastructural studies demonstrate the presence of **glutamate** in presynaptic terminals within the SCN. In situ hybridisation and immunocytochemical studies reveal the presence of several NMDA (NMDAR1, NMDAR2C), non-NMDA (GluR1, GluR2, GluR4) and metabotropic (mGluR1) **glutamate** receptor subunits in the SCN. Messenger RNA encoding a **glutamate** transporter protein is also present. In behavioural tests, **glutamate** antagonists can block the effects of light in phase-shifting circadian rhythms. Such treatments also block the induction

of c-fos within SCN cells by light, whereas a **glutamate** agonist (NMDA) induces c-fos expression. In hypothalamic slice preparations in vitro, electrical stimulation of the optic nerves induces release of **glutamate** and aspartate, and **glutamate** antagonists block field potentials in the SCN evoked by stimulation of the optic nerve. Circadian rhythms of electrical activity which persist in vitro are phase shifted by application of **glutamate** in a manner which mimics the phase shifting effects of light in vivo. This wide range of experimental findings provides strong support for the hypothesis that **glutamate** is the principal neurotransmitter within the **RHT**, and thus conveys photic cues to the circadian timing system in the SCN.

L18 ANSWER 10 OF 22 MEDLINE
ACCESSION NUMBER: 95385195 MEDLINE
DOCUMENT NUMBER: 95385195 PubMed ID: 7656420
TITLE: Developmental study in the circadian clock of the golden hamster: a putative role of astrocytes.
AUTHOR: Lavialle M; Serviere J
CORPORATE SOURCE: Laboratoire de Physiologie Sensorielle, INRA, Jouy-en-Josas, France.
SOURCE: BRAIN RESEARCH. DEVELOPMENTAL BRAIN RESEARCH, (1995 May 26) 86 (1-2) 275-82.
Journal code: DBR; 8908639. ISSN: 0165-3806.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951013
Last Updated on STN: 19951013
Entered Medline: 19951005

AB The hypothalamic suprachiasmatic nuclei (SCN) house the circadian clock in the mammalian brain. A glial fibrillary acidic protein immunoreactivity (GFAP-ir) distribution rhythm has been observed in the SCN of adult Syrian hamster. The implication of astrocytes in photic entrainment was analyzed through developmental studies of the photic pathway and of SCN astrocytes appearance. Using anterograde tracing we studied the timing of penetration of the retinohypothalamic tract (**RHT**) fibers into the SCN. Using c-fos induction by light we followed the maturation of **RHT** synapses in the SCN. When **RHT** terminals reach the SCN, c-fos induction can be obtained. Using GFAP immunoreactivity we demonstrated that the number of astrocytes increased in parallel with **RHT** development from PN5 to PN15. At PN15, a time when pups can shift from maternal to photic entrainment, **RHT** terminals and GFAP-ir exhibit an adult-like pattern. One demonstrated role of astrocytes is to control extracellular **glutamate** concentration. **Glutamate** is the neurotransmitter released at **RHT** terminals; its content fluctuates according to a circadian rhythm within the SCN. Thus the present data tend to indicate that SCN astrocytes are participating in the circadian rhythm of SCN **glutamate** content.

L18 ANSWER 11 OF 22 MEDLINE
ACCESSION NUMBER: 94306125 MEDLINE
DOCUMENT NUMBER: 94306125 PubMed ID: 7518323
TITLE: Responses of rat suprachiasmatic nucleus neurons to substance P and **glutamate** in vitro.
AUTHOR: Shirakawa T; Moore R Y
CORPORATE SOURCE: Department of Psychiatry, University of Pittsburgh, PA 15261.
CONTRACT NUMBER: NS-16304 (NINDS)
SOURCE: BRAIN RESEARCH, (1994 Apr 11) 642 (1-2) 213-20.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940825
Last Updated on STN: 19960129
Entered Medline: 19940816

AB The suprachiasmatic nucleus (SCN), a circadian pacemaker in the mammalian brain, receives photic information directly from the retina via the retinohypothalamic tract (**RHT**). Although the neurotransmitters of the **RHT** have not yet been identified, it is known that **glutamate** (Glu) and substance P (SP) are present in **RHT** axons. We report the responses of spontaneously firing SCN neurons to Glu and SP examined in isolated brain slices. 43% of the neurons show an excitatory response (an increase in firing rate) and 11% an inhibitory response to bath-applied SP at a concentration of 10(-7) M. Glu evokes excitatory responses from SCN neurons in a dose-dependent manner (10(-6)-10(-4) M). No day-night difference is observed in the response of SCN neurons either to 10(-7) M SP or to 10(-4) M Glu. Bath-applied SP has

additive effects on Glu-evoked responses and pressure-ejected SP at a concentration of 0.8 mM strongly potentiates Glu responses. These results are consistent with the view that Glu and/or SP function as neurotransmitters, or modulators, in the **RHT** and suggest that cellular processes downstream of the activation of SP or Glu receptors mediate time-dependent phase responses of SCN neurons.

L18 ANSWER 12 OF 22 MEDLINE
ACCESSION NUMBER: 93321091 MEDLINE
DOCUMENT NUMBER: 93321091 PubMed ID: 8101131
TITLE: **Glutamate** immunoreactivity in terminals of the retinohypothalamic tract of the brown Norwegian rat.
AUTHOR: de Vries M J; Nunes Cardozo B; van der Want J; de Wolf A; Meijer J H
CORPORATE SOURCE: Department of Physiology and Physiological Physics, University of Leiden, The Netherlands.
SOURCE: BRAIN RESEARCH, (1993 May 28) 612 (1-2) 231-7.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930826
Last Updated on STN: 19950206
Entered Medline: 19930813

AB The mammalian circadian pacemaker of the suprachiasmatic nucleus (SCN) is entrained to the environmental light-dark cycle via a retinal projection, the retinohypothalamic tract (**RHT**). Several studies suggest that an excitatory amino acid, possibly **glutamate**, is involved in photic entrainment. However, it has not yet been established whether **glutamate** is a transmitter of the **RHT** itself. We have now identified terminals of the **RHT** in the SCN of brown Norwegian rats by intravitreous injections of horse radish peroxidase conjugated to cholera toxin. To detect **glutamate** immunoreactivity (IR), post-embedding immunocytochemistry was performed with polyclonal antibodies which were visualized for electron microscopy with colloidal gold particles. Retinal terminals had a significantly 82% higher **glutamate**-IR than their post-synaptic dendrites and a significantly 76% higher **glutamate**-IR than non-retinal terminals. These observations provide ultrastructural evidence that **glutamate** is a transmitter of the **RHT**.

L18 ANSWER 13 OF 22 MEDLINE
ACCESSION NUMBER: 93214808 MEDLINE
DOCUMENT NUMBER: 93214808 PubMed ID: 8096424
TITLE: The effects of **glutamate** on membrane potential and discharge rate of suprachiasmatic neurons.
AUTHOR: Meijer J H; Albus H; Weidema F; Ravesloot J H
CORPORATE SOURCE: Department of Physiology, Leiden, The Netherlands.
SOURCE: BRAIN RESEARCH, (1993 Feb 19) 603 (2) 284-8.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930521
Last Updated on STN: 19950206
Entered Medline: 19930503

AB The suprachiasmatic nucleus (SCN) is a major pacemaker for circadian rhythms in mammals. Photic entrainment of the circadian pacemaker is mediated by the retinohypothalamic tract (**RHT**). Most likely, excitatory amino acids function as neurotransmitters in this pathway. We have now investigated the effect of **glutamate** on the membrane potential of cultured SCN cells of the rat with the aid of the patch clamp technique. It was found that 1 mM **glutamate** depolarizes the cells by about +44 mV. In spontaneously active neurons, the **glutamate** induced depolarization caused either an increase in discharge or a depolarization block. We then investigated the effect of 1 mM **glutamate** on SCN discharge in the acutely prepared hypothalamic slice of the hamster. In most cells **glutamate** induced an increase in discharge whilst in a few cells discharge was suppressed. Both series of experiments indicate that **glutamate** in the used dosage was effective and its effect reversible. The data are discussed with respect to the failure of 1 mM **glutamate** injections to mimic the effect of light on the circadian activity rhythm of the hamster.

L18 ANSWER 14 OF 22 MEDLINE
ACCESSION NUMBER: 92103242 MEDLINE
DOCUMENT NUMBER: 92103242 PubMed ID: 2979643

TITLE: The effects of intraventricular carbachol injections on the free-running activity rhythm of the hamster.
AUTHOR: Meijer J H; van der Zee E; Dietz M
CORPORATE SOURCE: Department of Behavioural Biology, University of Groningen, Haren, The Netherlands.
SOURCE: JOURNAL OF BIOLOGICAL RHYTHMS, (1988 Winter) 3 (4) 333-48.
Journal code: A9L; 8700115. ISSN: 0748-7304.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202
ENTRY DATE: Entered STN: 19920302
Last Updated on STN: 19920302
Entered Medline: 19920210

AB The effects of light on the circadian pacemaker in the suprachiasmatic nucleus (SCN) are mediated by the retinohypothalamic tract (**RHT**) and by the retinogeniculosuprachiasmatic tract (RGST). The neurotransmitter of the RGST is neuropeptide Y. The **RHT** may contain **glutamate** and aspartate. Recent evidence indicates that acetylcholine could also be involved in phase shifting by light. We determined that intraventricular injections with an acetylcholine agonist, carbachol, induces phase advances during the subjective day and phase delays during the early subjective night. No differences were observed between phase shifts induced in constant darkness and those induced in continuous light. A dose-response curve for carbachol was described at circadian time 6 (CT6). Injections at CT14 with various dosages of carbachol indicated the same dose dependency for this circadian time. Finally, carbachol injections in split animals resulted in similar responses of the two components of the split activity rhythm.

L18 ANSWER 15 OF 22 MEDLINE
ACCESSION NUMBER: 90123849 MEDLINE
DOCUMENT NUMBER: 90123849 PubMed ID: 2611651
TITLE: Retinohypothalamic tract stimulation activates thermogenesis in brown adipose tissue in the rat.
AUTHOR: Amir S
CORPORATE SOURCE: Department of Psychology, Concordia University, Montreal, Que., Canada.
SOURCE: BRAIN RESEARCH, (1989 Nov 27) 503 (1) 163-6.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19900328
Entered Medline: 19900314

AB We have shown that injecting **glutamate** into the hypothalamic suprachiasmatic nucleus (SCN) stimulates interscapular brown adipose tissue (IBAT) thermogenesis in rats. In the present study, electrical stimulation of the retinohypothalamic tract (**RHT**), a projection of retinal ganglion cell axons that course via the optic tract and terminate in the SCN, mimicked the effect of intra-SCN **glutamate** injection on IBAT thermogenesis. This effect could be blocked by prior injection of the local anesthetic procaine or the excitatory amino acid blockers kynurenic acid and delta-D-glutamylaminomethyl-phosphonic acid into the contralateral SCN, implicating the involvement of SCN **glutamate** receptors. The primary function of the **RHT** is to communicate photic information to the SCN, and it has been shown that **glutamate** might be involved in mediating this effect. On the basis of these observations and our finding of thermogenic responses to **RHT** stimulation or intra-SCN **glutamate**, we conclude that photic signals transmitted to the SCN via release of **glutamate** from the **RHT** might be capable of acutely modulating thermogenesis in IBAT.

L18 ANSWER 16 OF 22 MEDLINE
ACCESSION NUMBER: 89167685 MEDLINE
DOCUMENT NUMBER: 89167685 PubMed ID: 2538206
TITLE: Effects of excitatory amino acid receptor antagonists and agonists on suprachiasmatic nucleus responses to retinohypothalamic tract volleys.
AUTHOR: Cahill G M; Menaker M
CORPORATE SOURCE: Institute of Neuroscience, University of Oregon, Eugene 97403.
CONTRACT NUMBER: GM 07257 (NIGMS)
HD 13162 (NICHD)
SOURCE: BRAIN RESEARCH, (1989 Feb 6) 479 (1) 76-82.
Journal code: B5L; 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198904
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890428

AB A slice preparation of the mouse hypothalamus that includes the suprachiasmatic nuclei (SCN), the optic chiasm and the optic nerves was used for pharmacologic investigations of the nature of the receptors mediating the excitation of SCN neurons by input from the retinohypothalamic tract (**RHT**). Bath application of cis-2,3-piperidinedicarboxylic acid, a non-selective antagonist of excitatory amino acid receptors, reversibly blocked the postsynaptic component of the field potentials evoked in the dorsolateral SCN by stimulation of the optic nerve. The selective antagonist of N-methyl-D-aspartate receptors, 2-amino-5-phosphonovaleric acid, had no effect on SCN responses. **Glutamic acid** diethyl ester and 2-amino-4-phosphonobutyric acid also were without effect, but gamma-D-glutamylglycine caused a small decrease in the amplitude of the postsynaptic wave. Addition of the agonists, kainate and N-methyl-D,L-aspartate, to the superfusate also blocked the postsynaptic response. Kainate was the most potent agonist. L-**Glutamate** was without effect at up to 100 microM. These results indicate that postsynaptic responses in the SCN to retinohypothalamic tract volleys are mediated by a non-NMDA class of excitatory amino acid receptors.

L18 ANSWER 17 OF 22 MEDLINE
ACCESSION NUMBER: 88217073 MEDLINE
DOCUMENT NUMBER: 88217073 PubMed ID: 2897094
TITLE: **Glutamate** phase shifts circadian activity rhythms in hamsters.
AUTHOR: Meijer J H; van der Zee E A; Dietz M
CORPORATE SOURCE: Department of Zoology, University of Groningen, Haren, The Netherlands.
SOURCE: NEUROSCIENCE LETTERS, (1988 Mar 31) 86 (2) 177-83.
Journal code: N7N; 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19880617

AB The suprachiasmatic nuclei (SCN) have been identified as a pacemaker for many circadian rhythms in mammals. Photic entrainment of this pacemaker can be accomplished via the direct retino-hypothalamic tract (**RHT**). **Glutamate** is a putative transmitter of the **RHT**. In the present study it is demonstrated that **glutamate** injections in the SCN cause phase shifts of the circadian activity rhythm of the hamster. In contrast, **glutamate** injections outside the SCN or vehicle injections inside the SCN did not affect the circadian phase. These data suggest that **glutamate** could be involved in photic entrainment of the circadian pacemaker.

L18 ANSWER 18 OF 22 MEDLINE
ACCESSION NUMBER: 88139919 MEDLINE
DOCUMENT NUMBER: 88139919 PubMed ID: 3437073
TITLE: Retinohypothalamic projection and suprachiasmatic nucleus of the house sparrow, Passer domesticus.
AUTHOR: Cassone V M; Moore R Y
CORPORATE SOURCE: Department of Neurology, State University of New York, Stony Brook 11794.
CONTRACT NUMBER: NS-16304 (NINDS)
SOURCE: JOURNAL OF COMPARATIVE NEUROLOGY, (1987 Dec 8) 266 (2) 171-82.
Journal code: HUV; 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198803
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880325

AB The distribution of retinohypothalamic projections and the organization of the suprachiasmatic region of the hypothalamus was investigated in the house sparrow (Passer domesticus). Retinohypothalamic projections (**RHT**) were studied by two anterograde tracing methods, and hypothalamic organization was investigated immunohistochemically with antisera against a number of substances known to be present in the

mammalian suprachiasmatic nucleus (SCN): bombesin (BBS), **glutamic acid** decarboxylase (GAD), 5-hydroxytryptamine (5HT), neuropeptide Y (NPY), neurotensin (NT), somatostatin (SS), substance P (SP), vasoactive intestinal polypeptide (VIP), and arginine vasopressin (AVP). Observations from these experiments were analysed within the framework of a cytoarchitectural study using Nissl-stained material. From this study, we have identified an area in the anterior hypothalamus which we believe is an avian homologue of the mammalian SCN. This area contains a nucleus located in close apposition to the optic chiasm between the dorsal supraoptic decussation (DSD) and the ventral lateral geniculate body (GLv) for much of its rostrocaudal extent. The central portion of this nucleus contains neurons that exhibit GAD- and BBS-like immunoreactivity and is the terminal field for the **RHT**. For this reason, we term this nucleus the visual SCN. It also contains axon plexuses exhibiting 5HT-like, SP-like, and NPY-like immunoreactivity and is bordered ventrally by AVP-like, SP-like, and NT-like immunoreactive cells and medially by VIP-like and SS-like immunoreactive cells. Although it is not established that these cell groups together compose a single suprachiasmatic nucleus, the organization in the avian brain of a nuclear complex with a retinorecipient area surrounded by nonvisual components would be very similar to that of the mammalian SCN.

L18 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:64688 CAPLUS
DOCUMENT NUMBER: 124:144198
TITLE: The chemical composition of persimmon (Diospyros kaki, Thunb) leaf tea
AUTHOR(S): Joung, Seon-Young; Lee, Soo-Jung; Sung, Nak-Ju; Jo, Jong-Soo; Kang, Shin-Kwon
CORPORATE SOURCE: Dep. Food and Nutrition, Gyeongsang Natl. Univ., Jinju, 660-701, S. Korea
SOURCE: Han'guk Yongyang Siklyong Hakhoechi (1995), 24(5), 720-6
CODEN: HYSHDL; ISSN: 0253-3154
DOCUMENT TYPE: Journal
LANGUAGE: Korean
AB Chem. components relevant to the characteristic taste of the Korean native persimmon (Diospyros kaki) leaf tea were analyzed. Samples were processed by using three different methods; SHT (steamed and then hot-air dried), DHT (dried in the shade, steamed and then hot-air dried) and **RHT** (roasted and then hot-air dried). The components analyzed were general compns. of dried persimmon leaves and extd. soln. The compn. of moisture, ash, crude lipid and total nitrogen did not show significant variation among different processing methods of the persimmon leaf tea. The contents of caffeine, tannin and vitamin C in persimmon leaf tea were in the range of 178.4-209.8 .mu.mol/g, 29.1-38.5 mg% and 325.3-2084.7 mg%, resp. The vitamin C content was significantly higher in the **RHT** than other treatments. The contents of caffeine, tannin and vitamin C in the tea extd. soln. were in the range of 101.5-130.1 .mu.mol/g, 15.4-25.9 mg% and 111.0-1274.3 mg%, resp. The vitamin C in the tea soln. was the highest in the **RHT** treatment and 61.1% of vitamin C in the leaf tea was extd. out in these processing methods. The major amino acids contained in the leaf tea were in decreasing order **glutamic acid**, aspartic acid, leucine and phenylalanine, these four amino acids consisting 38.9-39.8% of the total amino acid contained in the persimmon leaf tea. The major amino acids contained in the tea soln. were **glutamic acid**, proline, histidine and arginine. Six kinds of 5'-nucleotides, CMP, AMP, UMP, IMP, GMP and hypoxanthine were detected and CMP was the most abundant component in the fresh leaf, leaf tea and tea soln. The second highest 5'-nucleotides in both leaf tea and tea solns. were GMP, AMP and UMP in all processing method. The highest free sugar contained in the fresh leaf tea and tea soln. was sucrose.

L18 ANSWER 20 OF 22 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:458865 BIOSIS
DOCUMENT NUMBER: PREV199799758068
TITLE: Pituitary adenylate cyclase-activating peptide (PACAP) in the retinohypothalamic tract: A potential daytime regulator of the biological clock.
AUTHOR(S): Hannibal, Jens (1); Ding, Jian M.; Chen, Dong; Fahrenkrug, Jan; Larsen, Philip J.; Gillette, Martha U.; Mikkelsen, Jens D.
CORPORATE SOURCE: (1) Dep. Clin. Biochemistry, Bispebjerg Hosp., Bispebjerg Bakke 23, DK-2400 Copenhagen NV Denmark
SOURCE: Journal of Neuroscience, (1997) Vol. 17, No. 7, pp. 2637-2644.
ISSN: 0270-6474.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The retinohypothalamic tract (**RHT**) relays photic information from the eyes to the suprachiasmatic nucleus (SCN). Activation of this pathway by light plays a role in adjusting circadian timing via a

glutamatergic pathway at night. Here we report a new signaling pathway by which the **RHT** may regulate circadian timing in the daytime as well. We used dual immunocytochemistry for pituitary adenylate cyclase-activating peptide (PACAP) and the in vivo tracer cholera toxin subunit B and observed intense PACAP-immunoreactivity (PACAP-IR) in retinal afferents in the rat SCN as well as in the intergeniculate leaflet (IGL) of the thalamus. This PACAP-IR in the SCN as well as in the IGL was nearly lost after bilateral eye enucleation. PACAP afferents originated from small ganglion cells distributed throughout the retina. The phase of circadian rhythm measured as SCN neuronal activity in vitro was significantly advanced (3.5 +- 0.4 hr) by application of 1 times 10-6 M PACAP-38 during the subjective day (circadian time (CT)-6) but not at night (CT14 and CT19). The phase-shifting effect is channeled to the clock via a PACAP-R1 receptor, because mRNA from this receptor was demonstrated in the ventral SCN by in situ hybridization. Furthermore, vasoactive intestinal peptide was nearly 1000-fold less potent in stimulating a phase advance at CT6. The signaling mechanism was through a cAMP-dependent pathway, which could be blocked by a specific cAMP antagonist, RpCAMPS, Thus, in addition to its role in nocturnal regulation by glutamatergic neurotransmission, the **RHT** may adjust the biological clock by a PACAP/cAMP-dependent mechanism during the daytime.

L18 ANSWER 21 OF 22 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999036700 EMBASE
TITLE: Pituitary adenylate cyclase activating peptide (PACAP) in the retinohypothalamic tract: A daytime regulator of the biological clock.
AUTHOR: Hannibal J.; Ding J.M.; Chen D.; Fahrenkrug J.; Larsen P.J.; Gillette M.U.; Mikkelsen J.D.
CORPORATE SOURCE: J. Hannibal, Department of Clinical Biochemistry, Bispebjerg Hospital, University of Copenhagen, DK-2400 Copenhagen NV, Denmark. biochbbh@inet.uni2.dk
SOURCE: Annals of the New York Academy of Sciences, (1998) 865/- (197-206).
Refs: 42
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
002 Physiology
003 Endocrinology
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The retinohypothalamic tract (**RHT**) relays photic information from the eyes to the brain biological clock in the suprachiasmatic nucleus (SCN). Activation of this pathway by light plays a role in adjusting circadian timing to light exposure at night. Here we report a new signaling pathway by which the **RHT** regulates circadian timing in the daytime as well. Using dual-immunocytochemistry for PACAP and the in vivo tracer Cholera toxin subunit B (ChB), intense PACAP immunoreactivity (PACAP-IR) was observed in retinal afferents at the rat SCN as web as in the intergeniculate leaflet (IGL) of the thalamus. This PACAP-IR was nearly lost upon bilateral eye enucleation. PACAP afferents originated from ganglion cells distributed throughout the retina. The phase of circadian rhythm measured as SCN neuronal activity in vitro was significantly advanced by application of PACAP-38 during the subjective day, but not at night. The effect is channelled to the clock via a PACAP 1 receptor-cAMP signaling mechanism. Thus, in addition to its role in nocturnal regulation by glutamatergic neurotransmission, the **RHT** can adjust the biological clock by a PACAP cAMP-dependent mechanism during the daytime.

L18 ANSWER 22 OF 22 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96019281 EMBASE
DOCUMENT NUMBER: 1996019281
TITLE: [Effects of complex phytosterol with or without T.H.S. on menopausal urogenital pathology].
EFECTOS ON LA PATOLOGIA UROGENITAL DE LA MENOPAUSIA DEL PHYTOSTEROL Y AMINOACIDOS CON/SIN T.H.S..
AUTHOR: Alvarez Alvarez P.; Martinez San Martin J.S.; Salazar Arquero F.J.
CORPORATE SOURCE: Unidad de Menopausia, Hospital Santa Cristina,28009 Madrid, Spain
SOURCE: Acta Ginecologica, (1995) 52/10 (313-316).
ISSN: 0001-5776 CODEN: ACGLAB
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
028 Urology and Nephrology
037 Drug Literature Index
LANGUAGE: Spanish

SUMMARY LANGUAGE: Spanish; English

AB A comparative study has been performed in 52 menopausal women showing various urinary symptoms falling into the concept of 'cystalgias-cystopathies'. Although the initial number of patients was 61, only the 52 patients appointed are included since there were 9 treatment withdrawals. Two control groups are established: GROUP A: included 24 women treated with phytosterol and aminoacids (complex phytosterol extracted from Prunus arborea, glycine, **glutamic acid** and alanine) and GROUP B: consisting of 28 women treated with the drug but who previously underwent Replacement Hormonal Therapy (**RHT**). Menopausal age, time to menopause and urinary symptoms as well as the evolution of symptoms during two months were compared and the effect of the drug either alone or associated with **RHT** was evaluated.